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<https://braininitiative.nih.gov/>

BRAIN Initiative Connectivity across Scales (BRAIN CONNECTS)

*Information for Applicants on Program
Goals, Application Instructions, and
Project Responsiveness*

BRAIN Initiative Connectivity across Scales (BRAIN CONNECTS)

Funding Opportunity Announcements (FOAs):

[RFA-NS-22-047](#) Comprehensive Centers for Human and NHP Brain (UM1)

[RFA-NS-22-048](#) Comprehensive Centers for Mouse Brain (UM1)

[RFA-NS-22-049](#) Specialized Projects for Scalable Technologies (U01)

Receipt Dates in July 2022 and June 2023

Email Contact: BRAIN-CONNECTS-Inquiries@nih.gov

Essential Information

- Read the FOAs carefully. The application instructions and review criteria are aligned with each other, and with the FOA goals, and will be the basis for peer review and programmatic funding decisions.
- All required information is contained in the FOAs. The following slides provide a summary but do not substitute for the FOAs.
- Alternative announcements from BRAIN or other programs may be more appropriate for your project.
- NIH staff can advise whether a potential application meets the FOA goals and BRAIN Initiative mission and can discuss potential alternatives.

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BRAIN CONNECTS Overview

- Coordinated Effort: aimed at developing the research capacity and technical capabilities to generate and interpret wiring diagrams, with goals of brain-wide coverage and comprehensive mapping
- Anticipated 10-Year Program: with the first 5 years focused on technology innovation, iterative engineering, and demonstration of feasibility
- Support for Complementary Approaches: with different technologies suited for different types of research questions and use-cases
- New Capabilities and New Discoveries: including new cell types, circuit motifs, wiring principles and circuit elements, and new computational and conceptual models based on rich new sources of data

Comprehensive Centers

- 5-year UM1 multi-component awards, 30-page research strategy
- Receipt dates in 2022 and 2023

[RFA-NS-22-047](#) **Comprehensive Centers for Human and NHP Brain**

Brain-wide coverage and comprehensive mapping of region-to-region connectivity at the level of axonal projections

[RFA-NS-22-048](#) **Comprehensive Centers for Mouse Brain**

Brain-wide coverage and comprehensive mapping of local and long-range cell-to-cell connectivity at the level of synaptic connections

Specialized Projects

- 3-year U01 single-component awards, 12-page research strategy
- Receipt dates in 2022, 2023 and 2024

[RFA-NS-22-049](#) **Specialized Projects for Scalable Technologies**

Budgets are not limited but must reflect the actual needs of the project

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[RFA-NS-22-049](#) Specialized Projects for Scalable Technologies

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Comprehensive Centers – Overall Goals

- *Research capacity and technical capabilities for brain-wide coverage and comprehensive mapping of neural connectivity.*
 - *Human and NHP: region-to-region connectivity at the level of axonal projections*
 - *Mouse: local and long-range cell-to-cell connectivity at the level of synaptic connections*
- *Large CNS sub-volumes sufficient to demonstrate feasibility and inform NIH decisions on program continuation in a subsequent five-year production period*
- *Establish and scale up complete pipelines, from sample collection through data integration and dissemination*
- *Advancing state-of-art methods and applying the data to research use-cases of high importance to the neuroscience community*

Comprehensive Centers – Application Instructions

Specific Aims:

Summarize overall goals and how the different components will be developed to demonstrate feasibility of scaling to entire brains in a potential subsequent five-year production period.

Research Strategy:

Center Overview (6 pages)

Overall Research Aims and Strategy, Organizational Structure, Administrative Support

Research Activities and Milestones (24 pages):

Divided into five research activity elements

For each element, explain the strategies and innovations that will:

- Enable scaling to high-throughput*
- Serve as a platform for mapping entire brains*
- Advance technologies and capabilities beyond current state-of-art*

Comprehensive Centers – Application Instructions

Research Activities and Milestones (24 pages):

1. Sample Processing and Data Acquisition

- *Provide details on tissue collection, processing, and sample handling, as well as imaging and/or other data acquisition modalities.*
- *Explain how these processes will be automated and scaled for high-throughput, including quality assurance and risk mitigation strategies.*
- *Additional species beyond human or NHP (NS-22-047) or mouse (NS-22-048) may be proposed for limited testing and optimization if justified in terms of scientific and cost benefits.*

Comprehensive Centers – Application Instructions

Research Activities and Milestones (continued):

2. Data Processing and Management

- *Describe the plan for data transfer, storage, and security across the different stages of the pipeline.*
- *Explain how performance will be assessed and optimized, including as appropriate, innovations from computer science and the information technology industry. Where possible, compatibility with existing resources should be prioritized.*
- *Detail the strategy for data processing steps, such as 3D registration and segmentation, annotation, error correction, and statistical representation.*
- *For automated analyses, explain how ground truth benchmarking will be accomplished and used for algorithm development, optimization, and accuracy assessment.*
- *Explain how the approach is well suited for efficient and cost-effective data processing and analysis, and how it will enable data integration into a wider data ecosystem within the BRAIN CONNECTS Network and beyond.*

Comprehensive Centers – Application Instructions

Research Activities and Milestones (continued):

3. Integration and Dissemination

Provide strategies and/or software toolsets for the following:

- *Integrating new data of the same modality*

Describe how new data will be incorporated and will serve to extend the overall dataset through additional detail and/or comparative information from additional subjects/animals.

- *Integrating across modalities into the wider knowledge base*

Explain how the Center data will complement other modalities, including molecular, morphological, connectivity, and/or functional data, for a unified understanding of brain cells, circuits, and networks.

- *Dissemination to the research community*

Describe how the Center data will be made available for easy access to the research community, including toolsets for collaborative proofreading, error correction, annotation, mining and discovery.

Comprehensive Centers – Application Instructions

Research Activities and Milestones (continued):

4. Research Discovery

- *For the chosen CNS volume, apply one or more key research use-cases to demonstrate the value of the data and the significance of the approach.*
- *Choose a scientific question(s) of high importance to the neuroscience community, for which understanding anatomical structure and connectivity will elucidate fundamental principles of neural function.*
- *If appropriate, functional experiments may be included (but are not required) to record and perturb circuit activity, provided the experiments are well-justified.*
- *The functional experiments must be limited in scope to complementing and further framing the significance of the corresponding connectivity data and should be integrated via computational and/or conceptual models with predictive outcomes.*

Comprehensive Centers – Application Instructions

Research Activities and Milestones (continued):

5. Feasibility Metrics and Milestones

- *Performance metrics for each of the first three research elements*
 - *Demonstrate feasibility of scaling to entire brains in a subsequent five-year period.*
 - *Enable comparison to other approaches.*
 - *Include expectations of cost, time, and any ancillary requirements*
- *Timeline and annual milestones*
 - *SMART criteria (Specific, Measurable, Attainable, Relevant, and Time-bound)*
 - *Separate delineation of:*
 - *Aspirational but realistic goals for the project*
 - *Go/no-go criteria representing minimally successful progress*

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[RFA-NS-22-049](#) Specialized Projects for Scalable Technologies

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Specialized Projects – Overall Goals

- *Proposals to develop current or emerging technologies for comprehensive atlases of brain connectivity, to enable faster, more precise, and more cost-effective generation and interpretation of brain-wide wiring diagrams.*
- *Emphasis on human, non-human primate (NHP), and mouse. Projects using other species are permitted if well-justified and the approaches can be generalized across species.*
- *Applications may address any aspect(s) of data collection, reconstruction, analysis, integration, dissemination, and interpretation of brain connectivity and associated data pipelines.*
- *Proposals are encouraged to develop distinct capabilities and competencies that may be expected to complement Comprehensive Centers solicited by the companion FOAs.*

Specialized Projects – Application Instructions

Specific Aims:

Explain how the project will contribute to scalable pipelines for brain connectivity and associated data.

Research Strategy (12 pages):

- *Detail how the project will:*
 - *Result in new or improved capabilities that can scale to whole brains*
 - *Advance current state-of-art, address gaps and challenges, and offer advantages over alternative methods.*
- *If a new dataset will be generated or analyzed, explain how it will contribute to novel research findings and/or new capabilities for the field.*
- *If using species other than mouse, NHP, or human, provide justification and explain how the approach can be generalized more broadly.*
- *Provide timeline and performance metrics to demonstrate feasibility of scaling to entire brains and for comparison to other approaches.*

Attachments (All FOAs)

Resource Sharing Plan

Plan for Enhancing Diverse Perspectives (PEDP):

- *One-page summary of strategies to advance the scientific and technical merit of the project through expanded inclusivity.*
- *Should provide a holistic and integrated view of how enhancing diverse perspectives is viewed and supported throughout the application.*
- *Will be evaluated according to multiple review criteria (Significance, Investigator(s), Innovation, Approach, and Environment), and can incorporate elements with relevance to any of these criteria*

For further guidance, FAQs, key elements, and examples, see:

<https://braininitiative.nih.gov/about/plan-enhancing-diverse-perspectives-pedp>

Applications lacking a PEDP attachment will be withdrawn without review

Non-Responsive Applications

Non-Responsive – Comprehensive Centers:

- *Projects not aimed at comprehensive pipelines for connectivity mapping in mouse, human or NHP*
- *Technologies not expected to provide comprehensive mapping of:*
 - *Region-to-region connectivity at the level of axonal projections in human or NHP*
 - *Local and long-range cell-to-cell connectivity at the level of synaptic connections in mouse*
- *Technologies not expected to demonstrate feasibility of scaling to atlases of entire brains in a potential subsequent five-year funding period*

Non-Responsive Applications

Non-Responsive – Specialized Projects:

- *Projects not aimed at developing or improving technologies that can serve as components of scalable pipelines for brainwide connectivity.*
- *Projects using approaches that will not be applicable to mammalian brain.*
- *Technologies not expected to provide comprehensive mapping of:*
 - *Region-to-region connectivity at the level of axonal projections in human or NHP.*
 - *Local and long-range cell-to-cell connectivity at the level of synaptic connections in mouse.*

Non-Responsive – All FOAs:

- *Applications lacking a PEDP submitted as Other Project Information as an attachment*

Special Review Criteria

- *In addition to the standard NIH review criteria, each FOA has Special Review Criteria listed under each of the scored elements.*
- *The Special Review Criteria are framed as questions for reviewers to assess in their evaluation of the proposal.*
- *They are closely matched to the application instructions for the Research Strategy, and for the PEDP and Resource Sharing Plan Attachments.*
- *The FOA goals, application instructions, and review criteria are all aligned, and will be considered in peer review and programmatic funding decisions – Read the FOAs Carefully*

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